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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,729	12/08/2004	Takeshi Nakanishi	441P088	6032

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EXAMINER	
ROGERS, JAMES WILLIAM	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/517,729	NAKANISHI ET AL.	
	Examiner	Art Unit	
	James W. Rogers, Ph.D.	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 5-7 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiply dependent claim. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Yokoyama et al. (US 6,080,396).

Yokoyama teaches a pharmaceutical preparation and the method to prepare it containing a copolymer of PEG and a poly amino acid which can include aspartic or glutameric acid as its monomers, the amino acid with a side chain carboxyl group that can be attached to an anthracyline-based anticancer agent. See abstract, col 3 lin 50-60. The process for producing the composition included dissolving the block copolymer in solvents such as water or water mixed with a low-boiling organic solvent along with the drug, the composition was then concentrated and freeze dried. See col 12 lin 53-col 13 lin 22 and examples. Regarding claims 5 and 7 Yokayama teaches using dimmers, trimers and tetramers of anthracylines such as adriamycin eg doxorubicin as well as drugs other than the dimmers, trimers and tetramers including adriamycin for

incorporation in the block copolymer, thus the limitations for anthracycline and doxorubicin are met.

Claims 1 and 3-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Yasuhisa et al. (EP 0,397,307 A2).

Sakurai teaches a water soluble block copolymer and the method to make it, the copolymer contains a hydrophobic segment that can contain PEG and a hydrophobic section that can contain polyaspartic acid and polyglutamic acid, the amino acid has a side chain carboxyl group that can be attached to an anthracyline-based anticancer agent including adriamycin eg doxorubicin. See abstract and pag 5 lin 3-14 and examples. The process for producing the composition included dissolving the block copolymer, adding the drug dissolved in DMF, then adding EDC and stirring the solution for 19 hours. Regarding claim 8 Sakurai teaches that the synthesized high molecular drug, despite the high adriamycin-substitution ratio, demonstrated good water solubility and kept its water solubility even when lyophilized or concentrated, therefore from this statement it is inherent that Sakurai lyophilized the copolymer-drug.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yokoyama et al. (US 6,080,396).

Yokoyama is disclosed above. The examples within Yokoyama disclose using dialysis and ultrafiltration on the reaction mixture in the process to form the drug containing copolymer. From the disclosure within Yokoyama it is obvious that other techniques could be employed besides dialysis or ultrafiltration because the patent states "replacing the solvent of the mixture solution with water by means of dialysis, ultrafiltration or the like", obviously shows that there are more ways to remove water encompassed within the patents scope. See col 12 lin 64-67. Besides the above argument the solvent employed can simply be water, therefore dialysis or ultrafiltration would not be a necessary step in the process to produce the pharmaceutical. From applicants own disclosure the step of not using dialysis or ultrafiltration was simply evaporating the solvent, since Yokoyama discloses low boiling solvents such as THF it would have been obvious to the skilled artisan to simply alloy the solution to dry by evaporation in order to concentrate the resulting solution. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yokoyama et al. (US 6,080,396) in view of Matsumara (Drug Delivery System, 16, No.

5, 401-408, 2001, disclosed as background art by applicants) in view of (JP-A No. 2001-226294, disclosed as background art by applicants).

Yokoyama is disclosed above. Yokoyama is silent on what methods other than using dialysis and ultrafiltration to prepare the drug containing copolymer.

Matsumara is used to show that it was known at the time of the invention that when dialysis or ultrafiltration are conducted on pharmaceuticals with contained drugs part of the drug is also removed, therefore the drug is not used effectively and the drug content cannot be increased. Therefore it would be obvious to use another technique to concentrate drugs instead of ultrafiltration and dialysis. See entire document especially experimental.

'294 is used only to show that producing a macromolecular block copolymer-drug composite by steps other than dialysis or ultrafiltration were already well known in the art. See entire document especially experimental.

It would have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to combine the art described in the documents above because Yokoyama discloses all of applicants claimed invention but is silent on what methods other than using dialysis and ultrafiltration to prepare the drug containing copolymer while from Matsumara one skilled in the art could see that another technique to concentrate substances with contained drugs besides ultrafiltration and dialysis should be employed to produce compositions with contained drugs and '294 showed that methods which did not employ dialysis or ultrafiltration in the production of a macromolecular block copolymer-drug such as simple evaporation were well known at

the time of the invention. The motivation to combine the above documents would be a general method to improve the drug loading of a block copolymer-drug containing a hydrophobic portion including PEG and a hydrophilic portion that includes polyamino acids that are covalently bonded through a condensation reaction with an anthracylcycline. Thus, the claimed invention, taken as a whole was *prima facie* obvious over the combined teachings of the prior art.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakurai et al. (EP 0,397,307 A2) in view of Matsumara (Drug Delivery System, 16, No. 5, 401-408, 2001, disclosed as background art by applicants) in view of (JP-A No. 2001-226294, disclosed as background art by applicants).

Sakurai is disclosed above. Yasuhisa is silent on what methods other than using dialysis and ultrafiltration to prepare the drug containing copolymer.

Matsumara is used to show that it was known at the time of the invention that when dialysis or ultrafiltration are conducted on pharmaceuticals with contained drugs part of the drug is also removed, therefore the drug is not used effectively and the drug content cannot be increased. See entire document especially experimental. Therefore it would be obvious to use another technique to concentrate drugs instead of ultrafiltration and dialysis.

294 is used only to show that producing a macromolecular block copolymer-drug composite by steps other than dialysis or ultrafiltration were already well known in the art. See entire document especially experimental.

It would have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to combine the art described in the documents above because Sakurai discloses all of applicants claimed invention but is silent on what methods other than using dialysis and ultrafiltration to prepare the drug containing copolymer while from Matsumara one skilled in the art could see that another technique to concentrate substances with contained drugs besides ultrafiltration and dialysis should be employed to produce compositions with contained drugs and '294 showed that methods which did not employ dialysis or ultrafiltration in the production of a macromolecular block copolymer-drug such as simple evaporation were well known at the time of the invention. The motivation to combine the above documents would be a general method to improve the drug loading of a block copolymer-drug containing a hydrophobic portion including PEG and a hydrophilic portion that includes polyamino acids that are covalently bonded through a condensation reaction with an anthracylcycline. Thus, the claimed invention, taken as a whole was *prima facie* obvious over the combined teachings of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No. 10/481,347. Although the conflicting claims are not identical, they are not patentably distinct from each other because both disclose the same block copolymer-drug composite comprised of a hydrophobic polymer (including PEG) moiety and a hydrophilic polyamino acid moiety, the amino acid is covalently attached to an anthracycline (including doxorubicin) and both disclose a process to produce or make the copolymer-drug composite that does not use dialysis nor ultrafiltration and the product can be in the form of a freeze dried product.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to James W. Rogers, Ph.D. whose telephone number is (571) 272-7838. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER